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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/397,957	09/17/99	DUONG H	A-65686-1

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EXAMINER	
LU, F	
ART UNIT	**PAPER NUMBER**
1655	6

DATE MAILED: 09/26/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/397,957	DUONG ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *Sequencing listing* .

DETAILED ACTION

Location of Application

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1655.

Drawings

2. The drawings are objected to for reasons as stated on FORM PTO-948 (Rev. 8-98). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Sequence Rules Compliance

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Direct the reply to the undersigned.

Claim Objections

4. Claim 4 is objected to because of the following informalities: Note that "JTFT" is abbreviation. It can only be used after phrase appears once.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting DNA hybridization wherein an array complex comprises oligonucleotides convalently attached to a plurality of electrodes, DNA target, and electron transfer moiety-ferrocene derivative, does not reasonably provide enablement for a method of detecting any target analytes in a sample wherein an array complex comprises any kind of capture binding ligand convalently attached to a plurality of electrodes, any kind of target analyte, and any kind of electron transfer moiety and a processing comprises a fast Fourier transform (FFT) analysis or a joint time-frequency transform (JTFT) or the use of a peak recognition scheme or a digital filter or a signal filter or a signal averaging or spectral analysis or peak recognition. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 547. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary & The Amount of Direction or Guidance Provided

Claims 1-10 in this instant application are directed to a method of detecting target analytes in a sample.

The claims have sufficient breadth of scope so to encompass a method of detecting any kind of target analyte in a sample wherein an array complex comprises any kind of capture binding ligand convalently attached to a plurality of electrodes, any kind of target analyte, and any kind of electron transfer moiety. The specification provides but limited guidance for a method of detecting DNA hybridization wherein an array complex comprises oligonucleotides convalently attached to a plurality of electrodes, DNA target, and electron transfer moiety-ferrocene derivative (pages 118-127). The specification, however, fails to provide guidance for a method of detecting any target analytes in a sample wherein an array complex comprises any kind of

capture binding ligand convalently attached to a plurality of electrodes, any kind of target analyte, and any kind of electron transfer moiety which the claims are directed to.

Note that although the specification provides a seies of formula, the specifcation fails to provide adequate guidance to use these formula in a method of detecting any target analytes in a sample wherein a processing comprises a fast Fourier transform (FFT) analysis or a joint time-frequency transform (JTFT) or the use of a peak recognition scheme or a digital filter or a signal filter or a signal averaging or spectral analysis or peak recognition.

With the specification exemplifying but a method of detecting DNA hybridization wherein an array complex comprising oligonucleotides convalently attached to a plurality of electrodes, DNA target, and electron transfer moiety- ferrocene derivative, and suggesting other methods, the skilled artisan is left to extrapolate a method of detecting DNA hybridization wherein an array complex comprising oligonucleotides convalently attached to a plurality of electrodes, DNA target, and electron transfer moiety- ferrocene derivative to a method of detecting any kind of target analyte in a sample wherein an array complex comprising any kind of capture binding ligand convalently attached to a plurality of electrodes, any kind of target analyte, and any kind of electron transfer moiety.

Clearly, there will be a lot of unpredictable factors when the skilled artisan extrapolate a method of detecting DNA hybridization wherein an array complex comprising oligonucleotides convalently attached to a plurality of electrodes, DNA target, and electron transfer moiety-ferrocene derivative to a method of detecting any kind of target analyte in a sample wherein an array complex comprises any kind of capture binding ligand convalently attached to a plurality of

electrodes, any kind of target analyte, and any kind of electron transfer moiety and a processing comprises a fast Fourier transform (FFT) analysis or a joint time-frequency transform (JTFT) or the use of a peak recognition scheme or a digital filter or a signal filter or a signal averaging or spectral analysis or peak recognition so that the skilled artisan will have no way to predict the experimental results. Such efforts constitute undue experimentation.

The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects

of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research."

The Presence or Absence of Working Examples

The specification (pages 118-127) provides working examples for: (1) general methods of making substrates and monolayers; (2) detection of target sequences by hybridization; and (3) the use of FFT and JTFT for signal proceesing.

The Nature of the Invention

The invention relates to a method of detecting target analytes in a sample.

The State of the Prior Art

At the time of filling, an oligonucleotide array constructed on a silicon device bearing a matrix of addressable 50-microns microelectrodes has been used for DNA hybridization (Livache *et al.*, Anal. Biochem. 255, 188-194, January 1998). However, a method of detecting any kind of target analyte in a sample wherein an array complex comprises any kind of capture binding ligand convalently attached to a plurality of electrodes, any kind of target analyte, and any kind of electron transfer moiety and a processing comprises a fast Fourier transform (FFT) analysis or a joint time-frequency transform (JTFT) or the use of a peak recognition scheme or a digital filter or a signal filter or a signal averaging or spectral analysis or peak recognition is a novel and an undeveloped area of the art.

The Relative Skill of Those in the Art

The relative skill of those in the art to which the invention most closely pertains is high, on par with those which hold a Ph.D. in biochemistry.

The Predictability or Unpredictability of the Art

Based on the limited guidance provided by the specification (pages 118-127), a skilled artisan can perform a method of detecting DNA hybridization wherein an array complex comprising oligonucleotides convalently attached to a plurality of electrodes, DNA target, and electron transfer moiety- ferrocene derivative. However, it is unpredictable whether a skilled artisan can perform a method of detecting any kind of target analyte in a sample wherein an array complex comprises any kind of capture binding ligand convalently attached to a plurality of electrodes, any kind of target analyte, and any kind of electron transfer moiety and a processing comprises a fast Fourier transform (FFT) analysis or a joint time-frequency transform (JTFT) or the use of a peak recognition scheme or a digital filter or a signal filter or a signal averaging or spectral analysis or peak recognition. Therefore, the predictability of the art is low. Further, the claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable

> factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The Breadth of the Claims

The claims encompass a method of detecting any kind of target analyte in a sample wherein an array complex comprising any kind of capture binding ligand convalently attached to a plurality of electrodes, any kind of target analyte, and any kind of electron transfer moiety. In view of the limited guidance and the acknowledged areas of difficulty, applicant is urged to consider narrowing the scope of the claims to that which attention has been directed.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims 1-10 are rejected as vague and indefinite over " a first input signal" in step (b) of claims 1 and 10 because it is unclear what kind of signal will be define as " a first input signal". For the examination purpose, " a first input signal" is considered as a light signal such as light excitation. This rejection can be overcome by clarifying this subject matter.

9. The term "higher harmonic analysis " in claim is a relative term which renders the claim indefinite. The term "higher harmonic analysis" is not defined by the claim, the specification does

not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 U.S.C. § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --

11. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Livache *et al.*, (Anal. Biochem. 255, 188-194, January 1998).

Livache *et al.*, teach an oligonucleotide array constructed on a silicon device bearing a matrix of addressable 50-microns microelectrodes. The 48 individually addressable 50×50 -μm^2 gold electrodes were arranged in a 4×12 matrix (page 189, left column, second paragraph). Each electrode was covered by a conducting polymer (polypyrrole) grafted by an oligonucleotide (ODN). The DNA chip was prepared by successive electrochemically addressed copolymerizations of 5' pyrrole-labeled ODN and pyrrole (page 188, abstract). Following hybridization of the biotinylated amplified sample on the chip bearing a series of probes, detection was carried out by fluorescence microscopy through an R-phycoerythrin label. Note that absorption and emission of R-phycoerythrin are considered as an input and output signals here. The prior art meets the limitations of the claim.

Conclusion

10. No claim is allowed.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank L., Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
September 22, 2000

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600